



# **Armed Forces College of Medicine AFCM**





# **Neuro muscular junction**

**“Motor End Plate MEP”**

**Ass. Prof. Mona Gamal El Din Al**

**Anan**

**Neuromuscular  
Junction**



# INTENDED LEARNING OBJECTIVES (ILO)

**By the end of this lecture the student will be able to:**

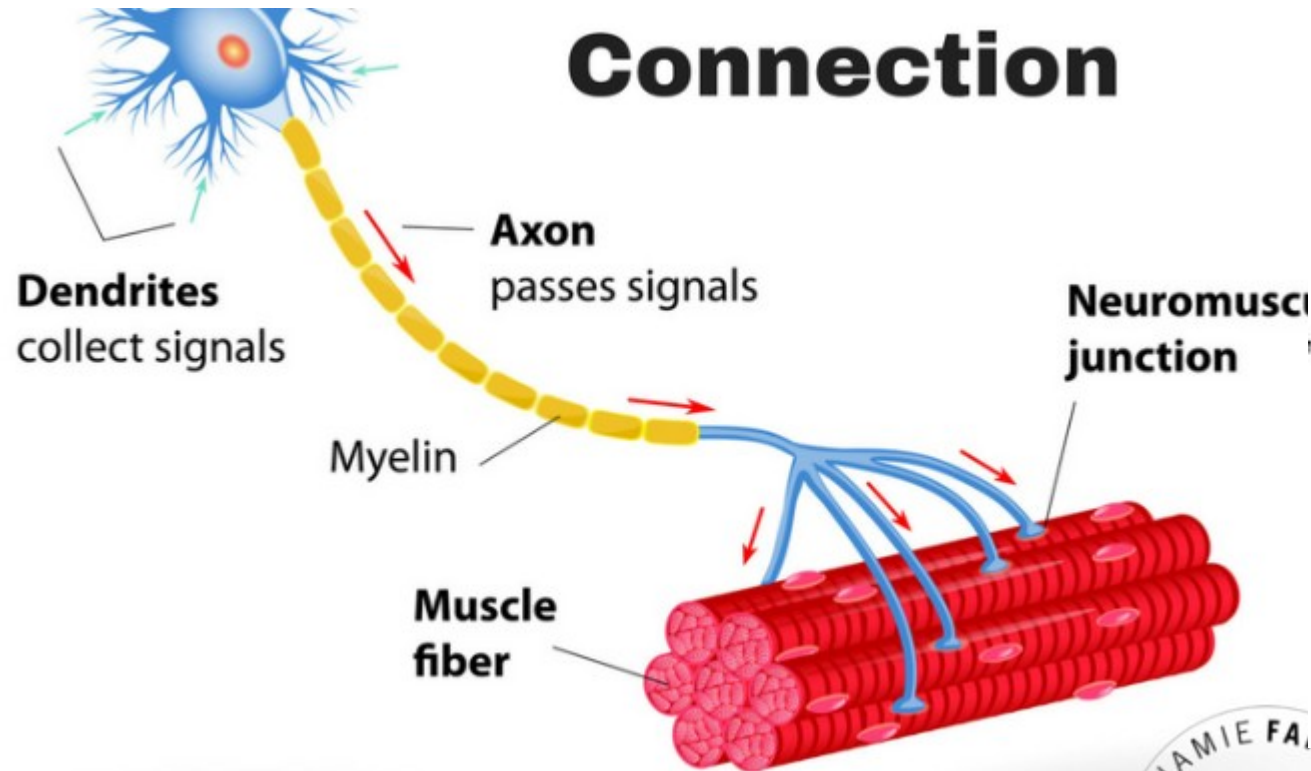
1. Describe the physiological anatomy of the neuromuscular junction
2. Explain the mechanism of neuromuscular transmission
3. Describe the properties of neuromuscular transmission
4. Explain the pathophysiology of Myasthenia gravis



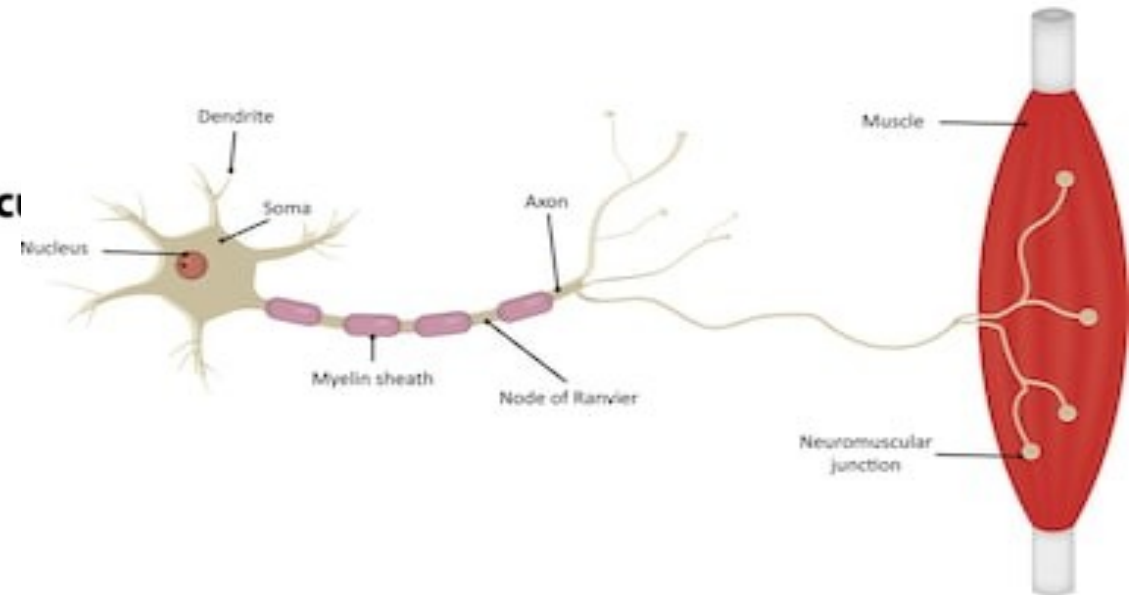
# Neuromuscular junction = Motor end plate “MEP”



## Connection



## Motor Neuron



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<https://perch.fit/images/blog/anatomy/motor-unit.png>

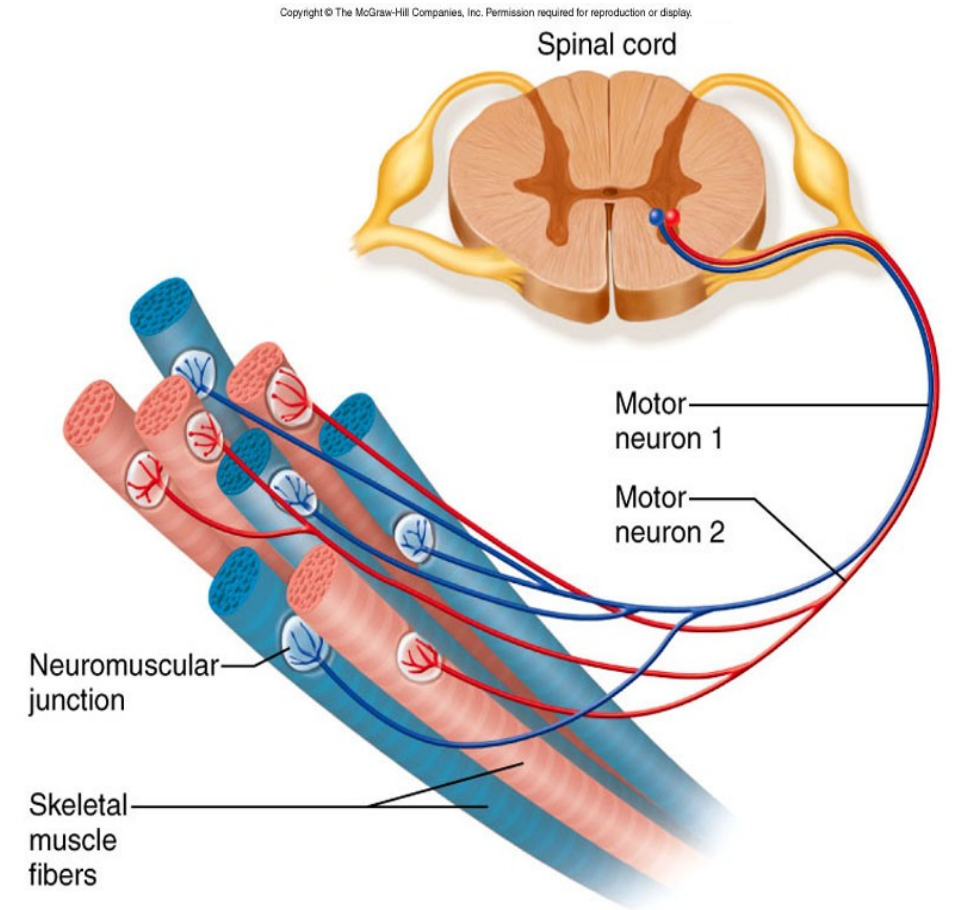
<https://image.shutterstock.com/image-vector/motor-neurone-labeled-260nw-311314823.jpg>



# Neuromuscular junction = Motor end plate “MEP”



- ❖ Skeletal muscles are innervated by large myelinated nerve fibers, originating from the large motor neurons of the anterior horn cell of the spinal cord
- ❖ Each nerve fiber branches many times to stimulate several skeletal muscle fibers



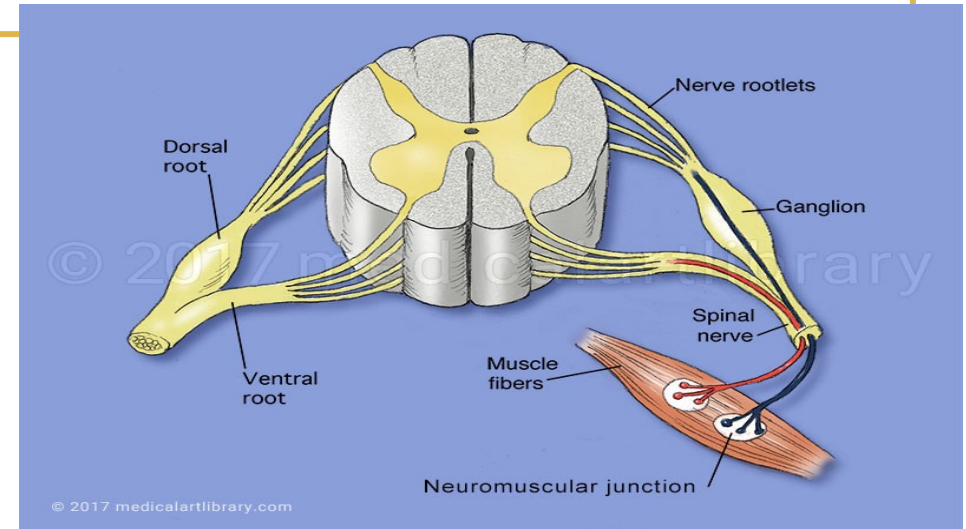
[https://deansomerset.com/wp-content/uploads/2015/02/f11-05\\_motor\\_c.jpg](https://deansomerset.com/wp-content/uploads/2015/02/f11-05_motor_c.jpg)



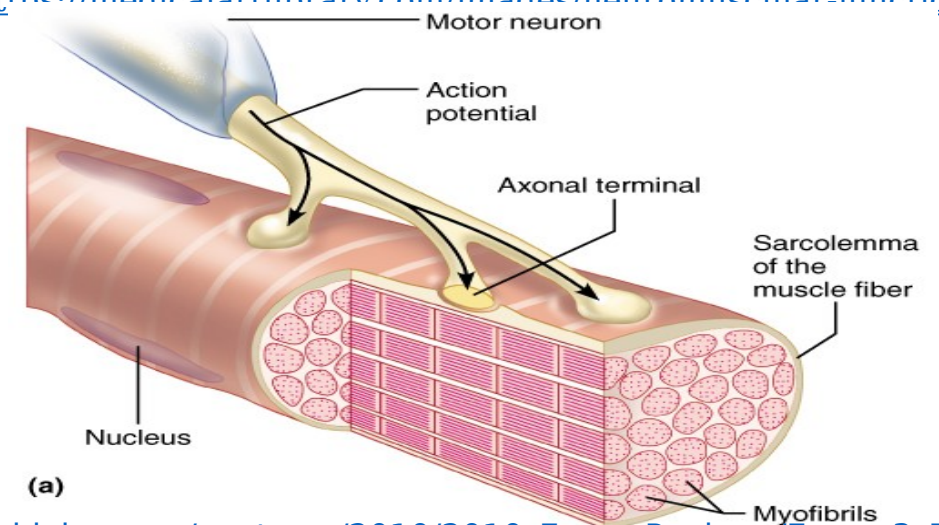
# Neuromuscular junction = Motor end plat “MEP”



❖ The site of junction between nerve and skeletal muscle fibers is called **neuromuscular junction**, which is mostly at the fibers mid point, so that the action potential travels in both directions



<https://medicalartlibrary.com/images/neuromuscular-junction.jpg>



[https://www.apsbiology.org/anatomy/2010/2010\\_Exam\\_Reviews/Exam\\_3\\_Review/CH\\_09\\_Motor\\_Unit\\_and\\_Neuromuscular\\_Junction.htm](https://www.apsbiology.org/anatomy/2010/2010_Exam_Reviews/Exam_3_Review/CH_09_Motor_Unit_and_Neuromuscular_Junction.htm)



# Neuromuscular junction = Motor end plate “MEP”

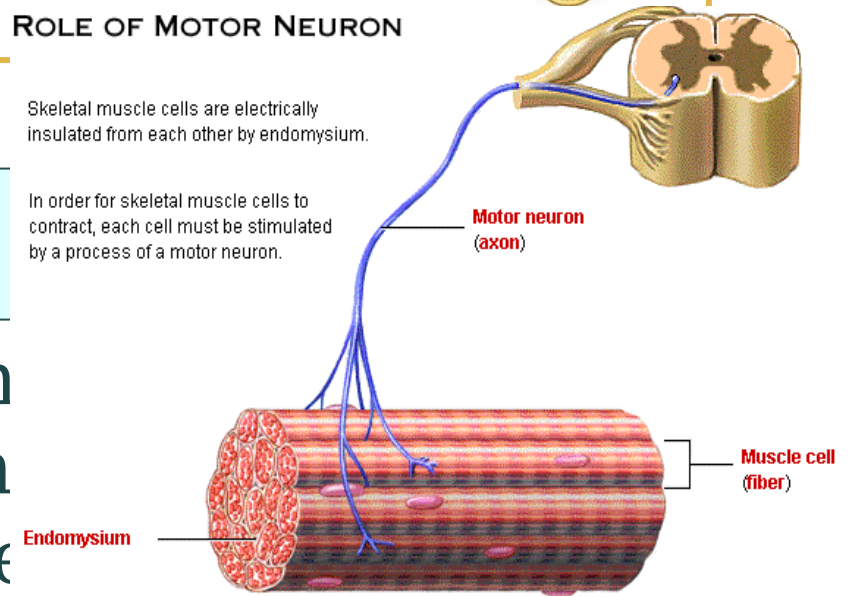
An action potential in a motor neuron rapidly spreads from the CNS to the skeletal muscle through the axon

As the axon approaches the muscle it divides into many terminal branches and loses its myelin sheath

## ROLE OF MOTOR NEURON

Skeletal muscle cells are electrically insulated from each other by endomysium.

In order for skeletal muscle cells to contract, each cell must be stimulated by a process of a motor neuron.



Each of these axon terminals forms the neuromuscular junction with one of many muscle fibers



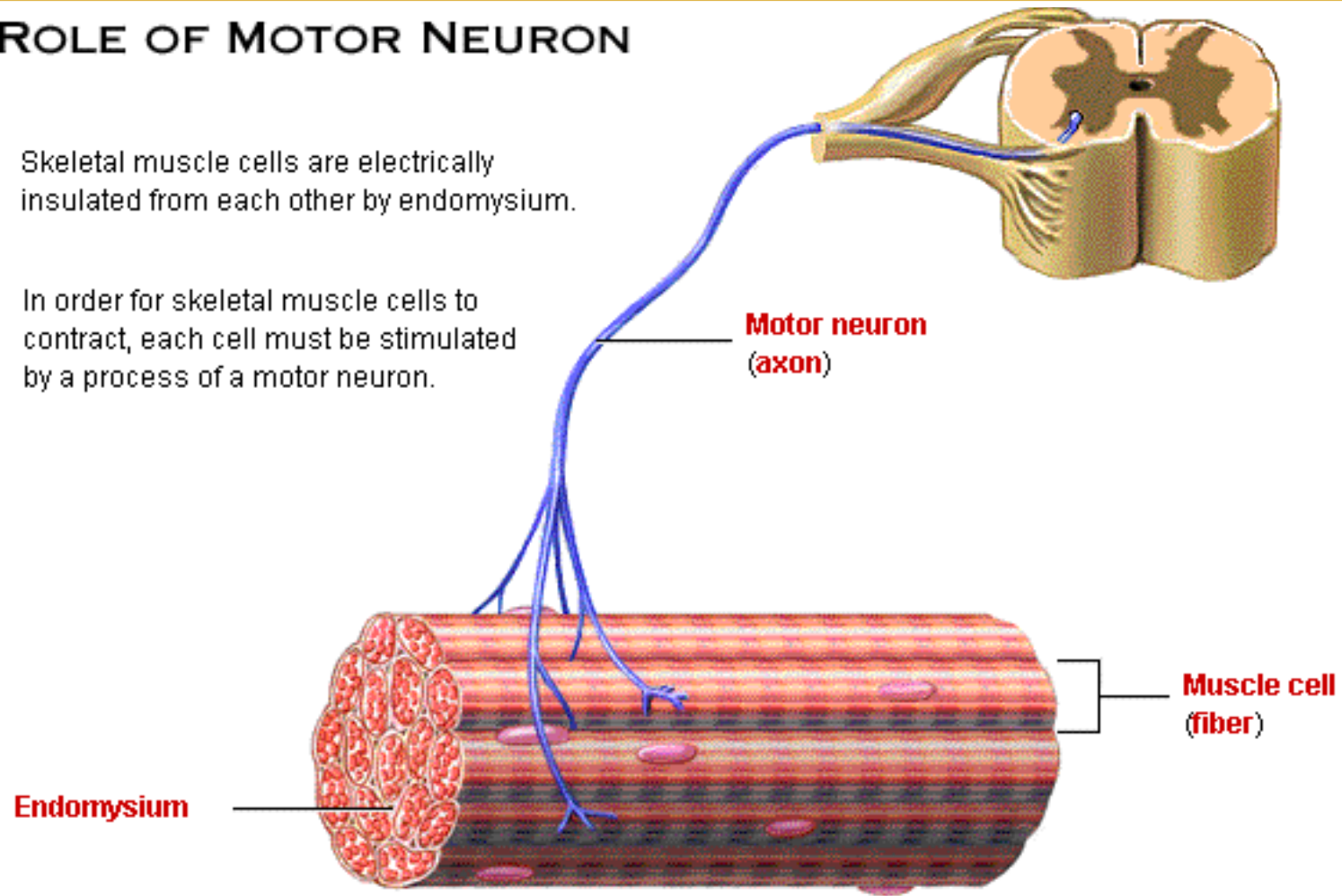
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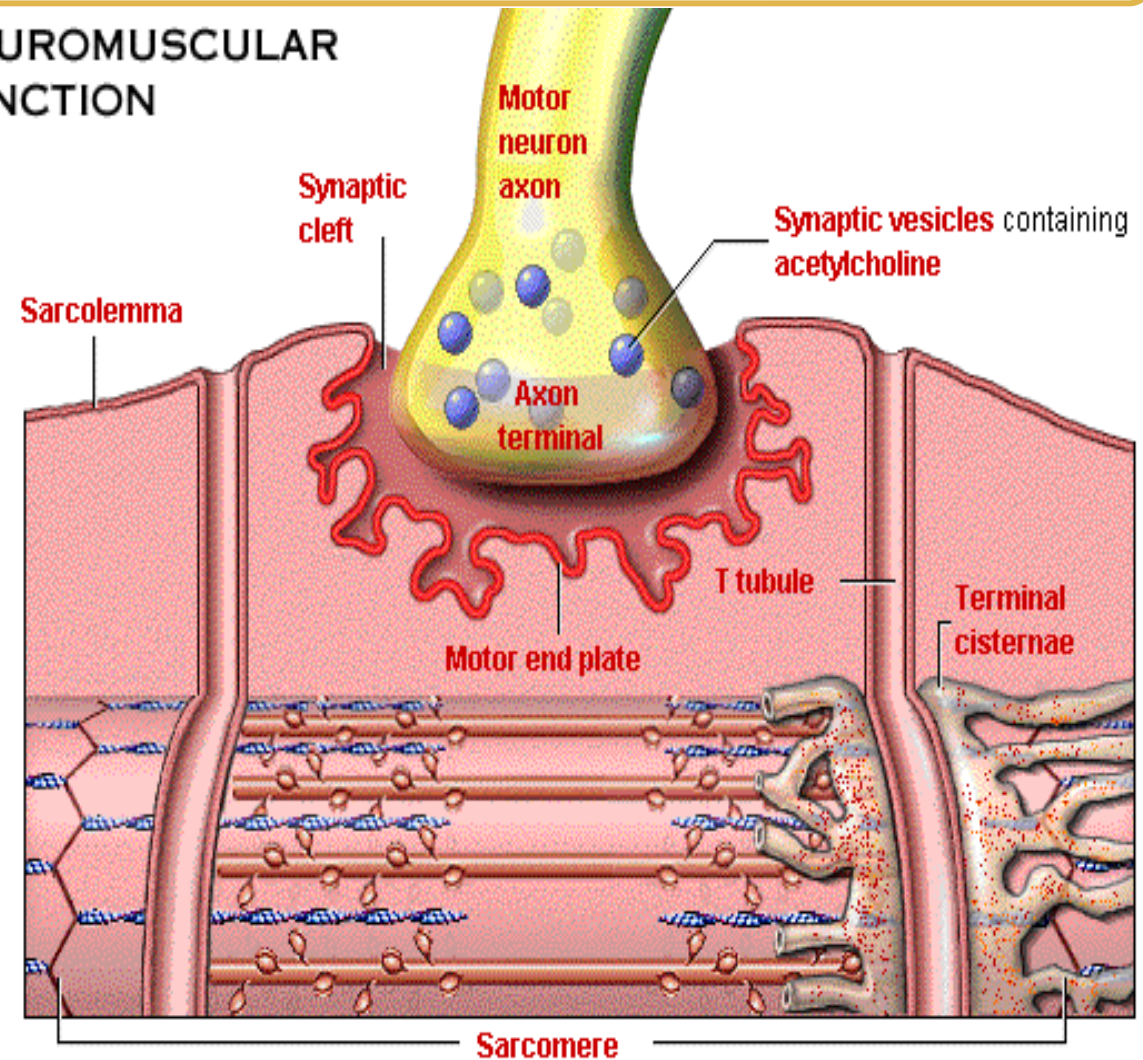
# Neuromuscular junction = Motor end plate “MEP”



The axon terminal is enlarged into a knob like structure, the terminal button

The terminal button fits into a shallow depression in the underlying muscle fiber

NEUROMUSCULAR JUNCTION



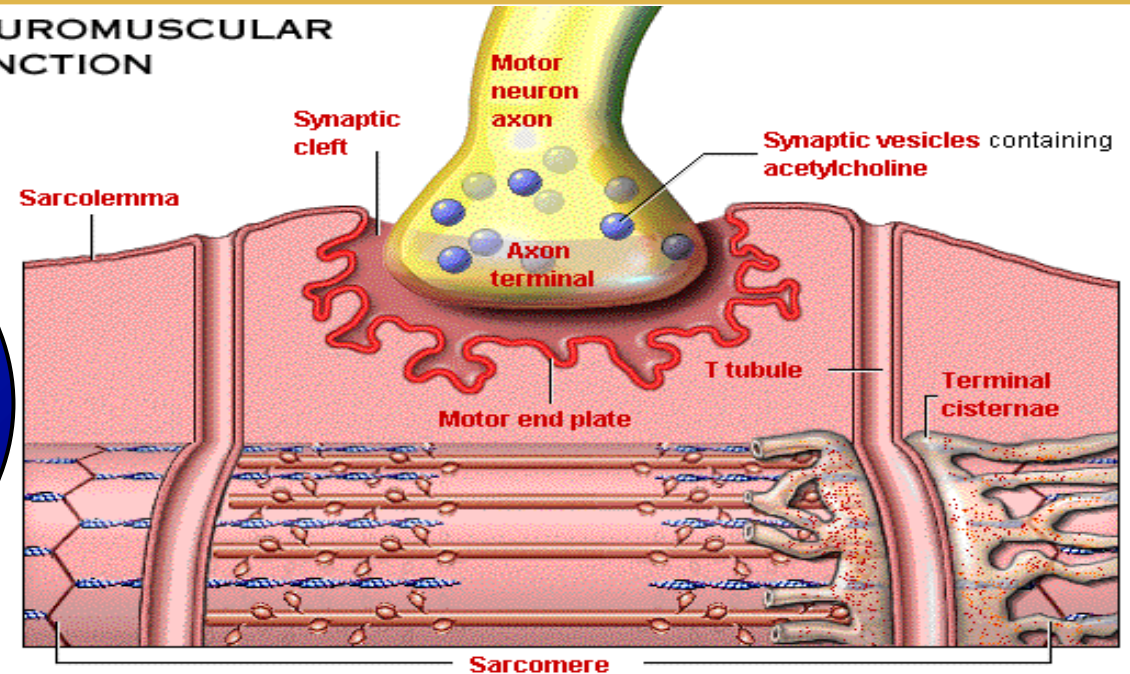


# Neuromuscular junction = Motor end plate “MEP”



The specialized portion of the muscle cell membrane immediately under the terminal button is known as the Motor End Plate

NEUROMUSCULAR JUNCTION



N.B:  
Nerve and muscle cell do not come into direct contact at neuromuscular junction



# Neuromuscular junction = Motor end plate “MEP”



The nerve fiber branches at its end to form nerve terminals called **the end plate**, which invaginates into the muscle fiber, but it lies outside the cell membrane (no cytoplasmic continuity between the nerve terminals and muscle fibers)



# Neuromuscular junction = Motor end plate “MEP”

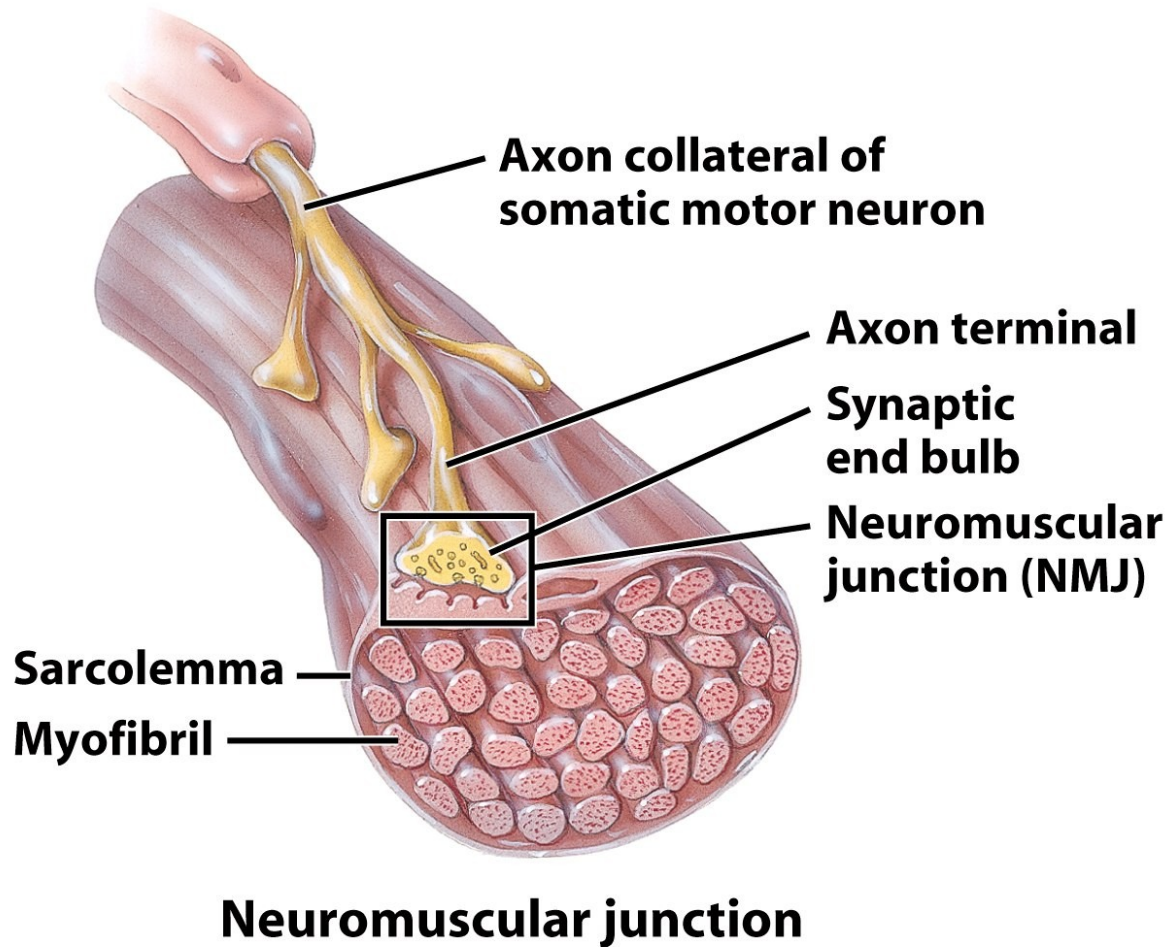


Figure 10-10a Principles of Anatomy and Physiology, 11/e  
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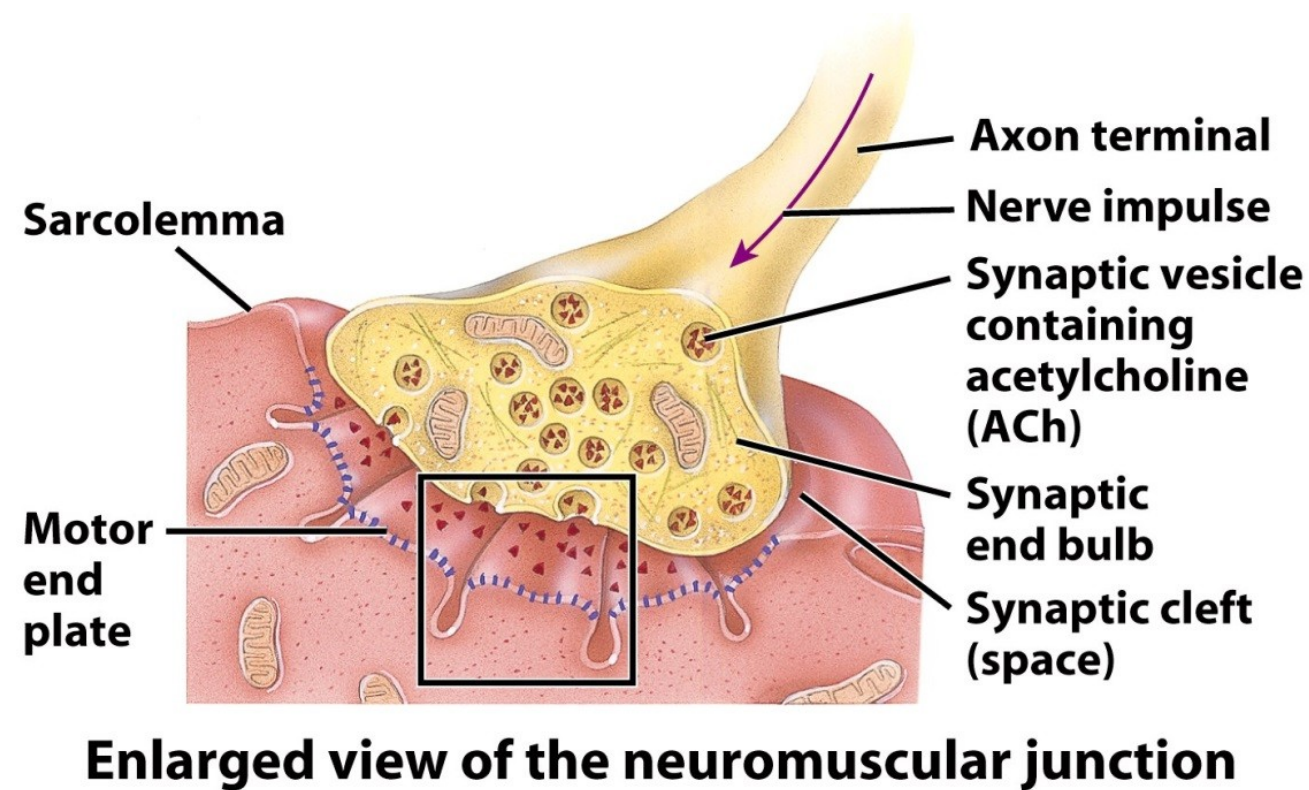
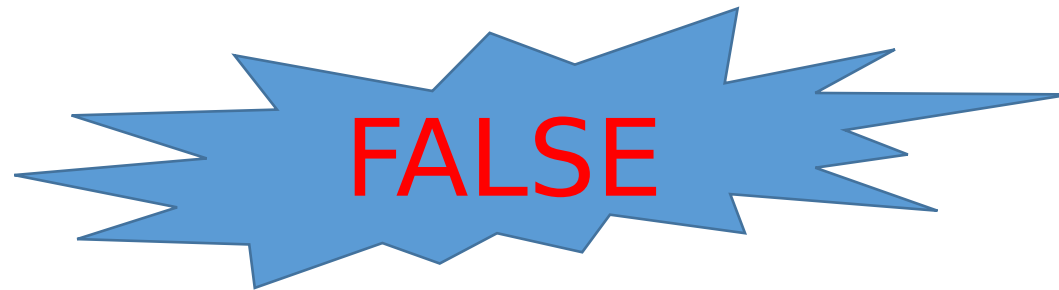


Figure 10-10b Principles of Anatomy and Physiology, 11/e  
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# True Or False

- There is a cytoplasmic continuity between the nerve terminals and muscle fibers



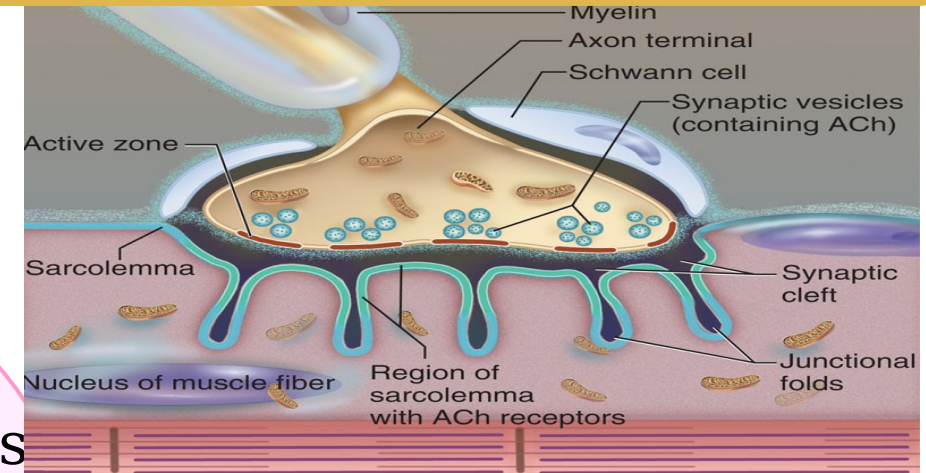


# Neuromuscular junction = Motor end plate “MEP”



There is a space or cleft between nerve and muscle cells at neuromuscular junction

Each terminal button contains thousands of vesicles that store chemical transmitter acetylcholine



When action potential reaches axon terminal the voltage-gated  $\text{Ca}^{++}$  channels in the terminal button open up

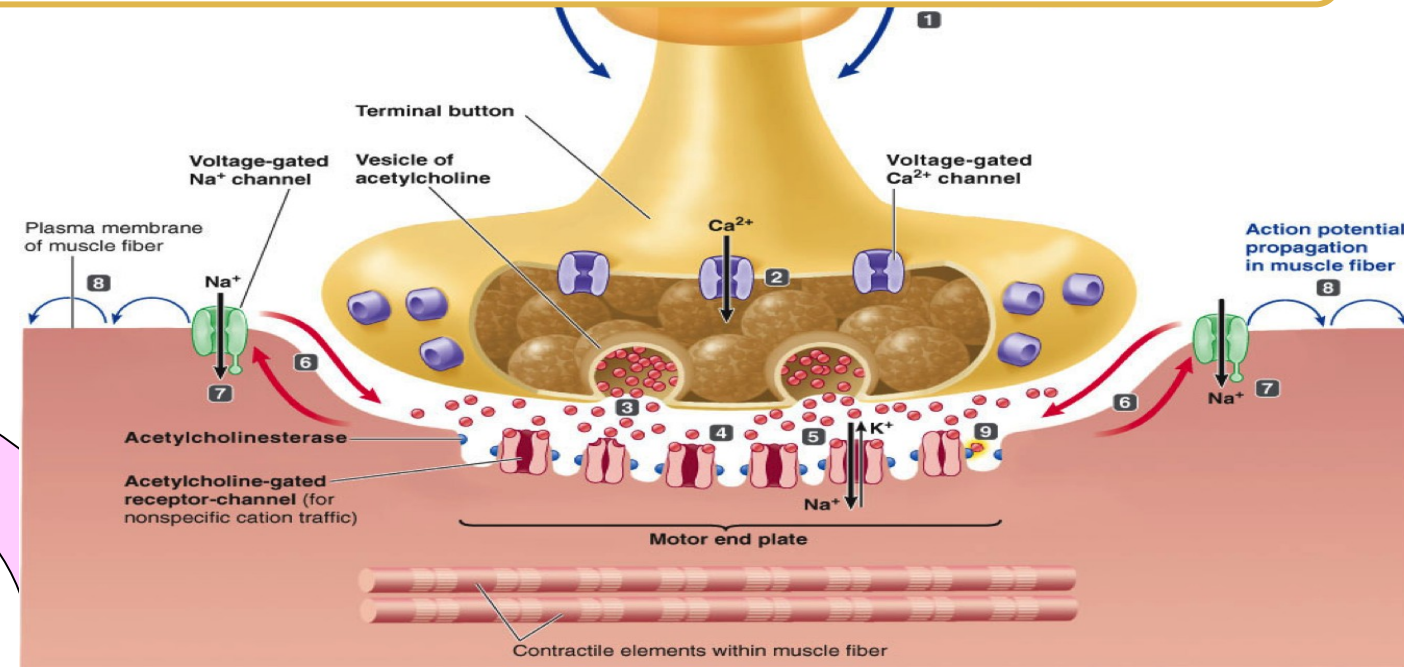


# Neuromuscular junction = Motor end plate “MEP”



This permits  $\text{Ca}^{++}$  to diffuse into the terminal button from its higher extracellular concentration

Diffusion of  $\text{Ca}^{++}$  into the terminal button causes release of ACh from vesicles into the cleft



The ACh in the cleft binds with specific receptor sites which are unique to the motor end plates

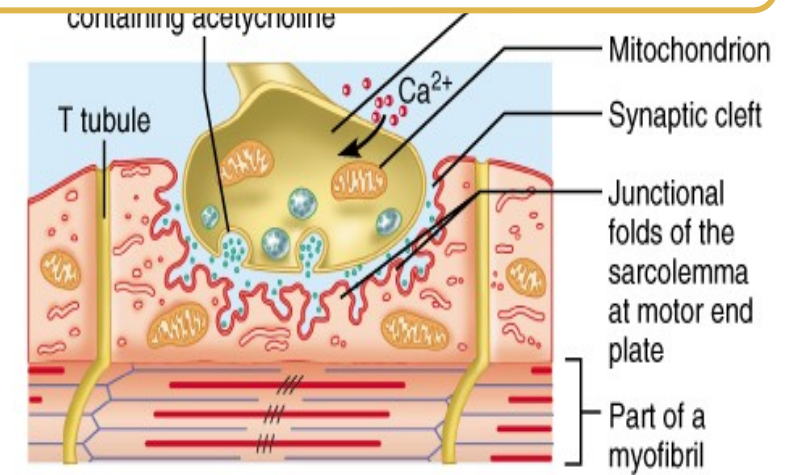


# Neuromuscular junction = Motor end plate “MEP”



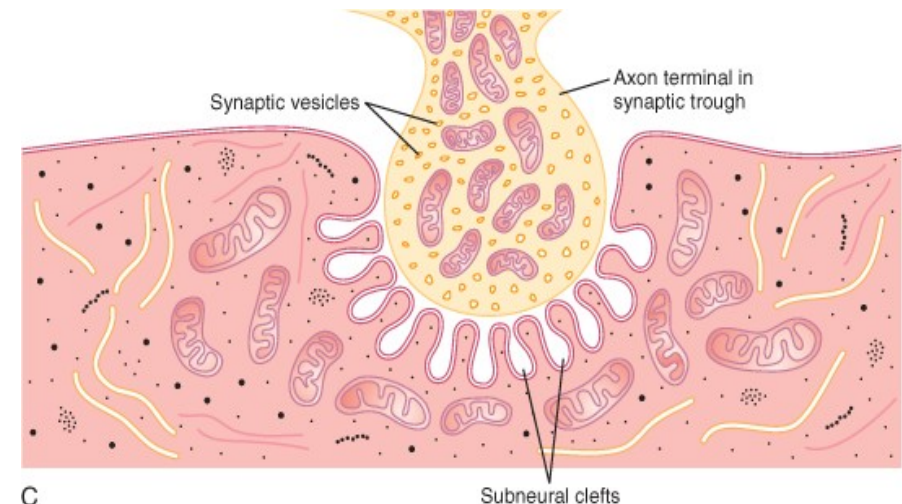
of

The space between the nerve terminals and muscle is called **synaptic cleft**, it is filled with a lot of **cholinesterase enzyme**. There are many **mitochondria** in the axon terminals that supply energy mainly for synthesis of an excitatory transmitter, **acetylcholine**, in the cytoplasm of the nerve terminals and rapidly absorbed into many **synaptic vesicles**.



(b)

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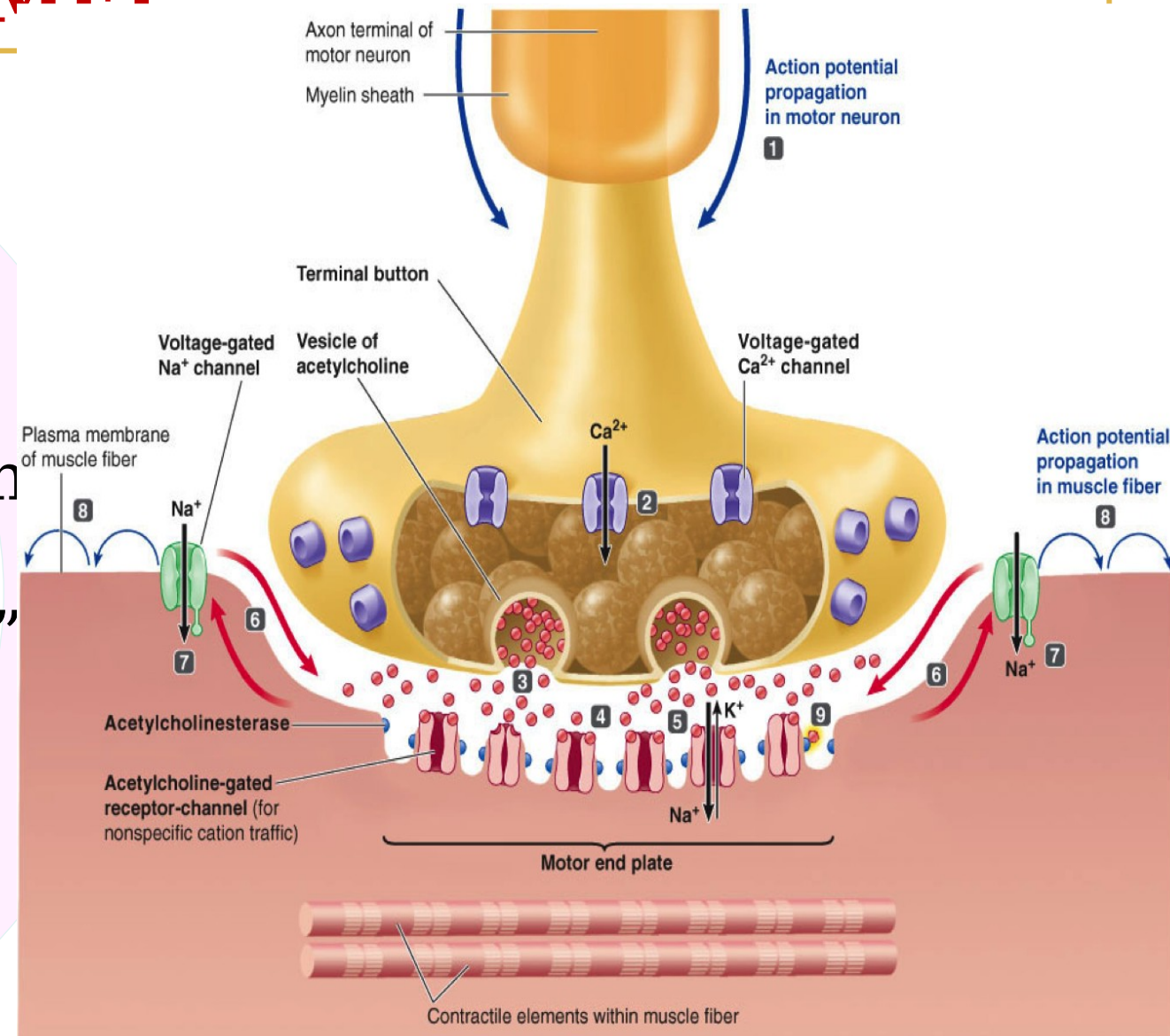
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# Neuromuscular junction = Motor end plate “MFP”



Binding of Ach with these receptors (nicotinic) causes opening of non selective cation channels □ generation of a local “graded” potential at the end plate known as end plate potential (EPP)



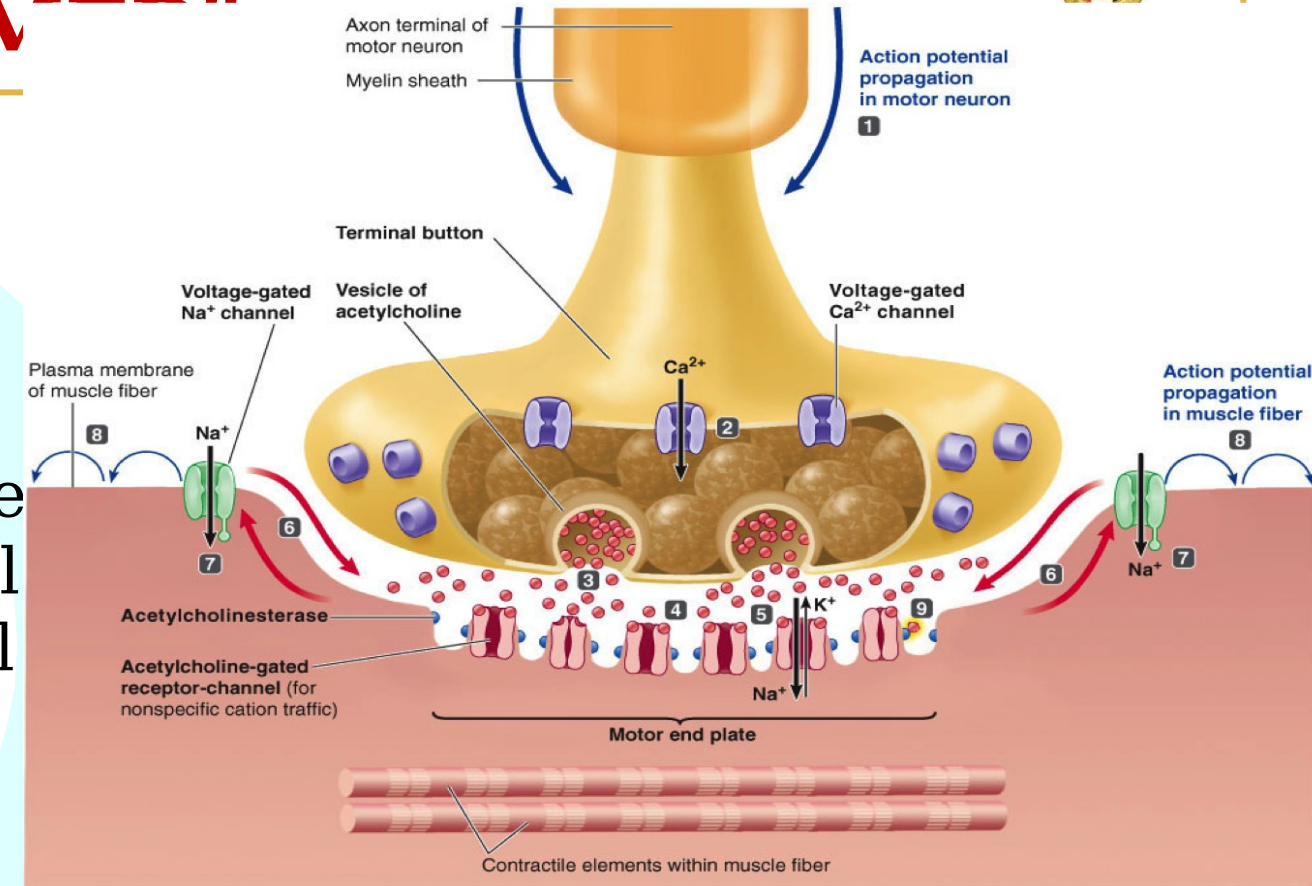


# Neuromuscular junction = Motor end plate



“N”

The EPP later on brings about local current flow in the adjacent area, reducing their membrane potential to firing where an action potential is generated and spread in the rest of the muscle membrane.



Each action potential in nerve generates action potential in muscle



# End plate potential (EPP)



- Sudden entry of sodium ions into the muscle fiber decrease the membrane potential in the local area of the end plate, creating a local potential called the end plate potential (Partial depolarization of the membrane)
- The end plate potential is a local unpropagated potential, when it reaches certain value called threshold potential it fires the potential on both sides of the motor end plate,

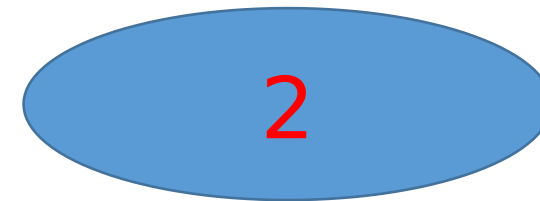


# Choose the correct answer

- The end plate potential is .....

1. a local potential

2. an action potential

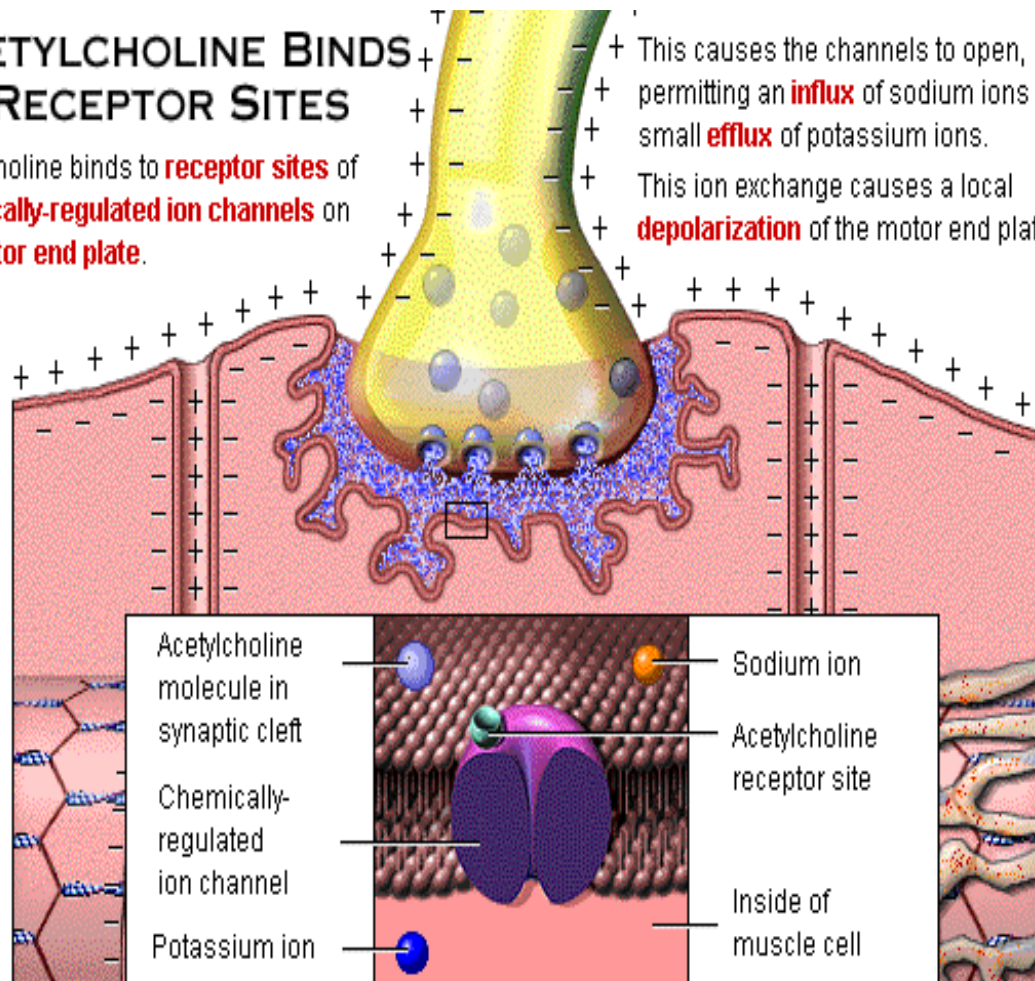




## ACETYLCHOLINE BINDS TO RECEPTOR SITES

Acetylcholine binds to **receptor sites** of **chemically-regulated ion channels** on the **motor end plate**.

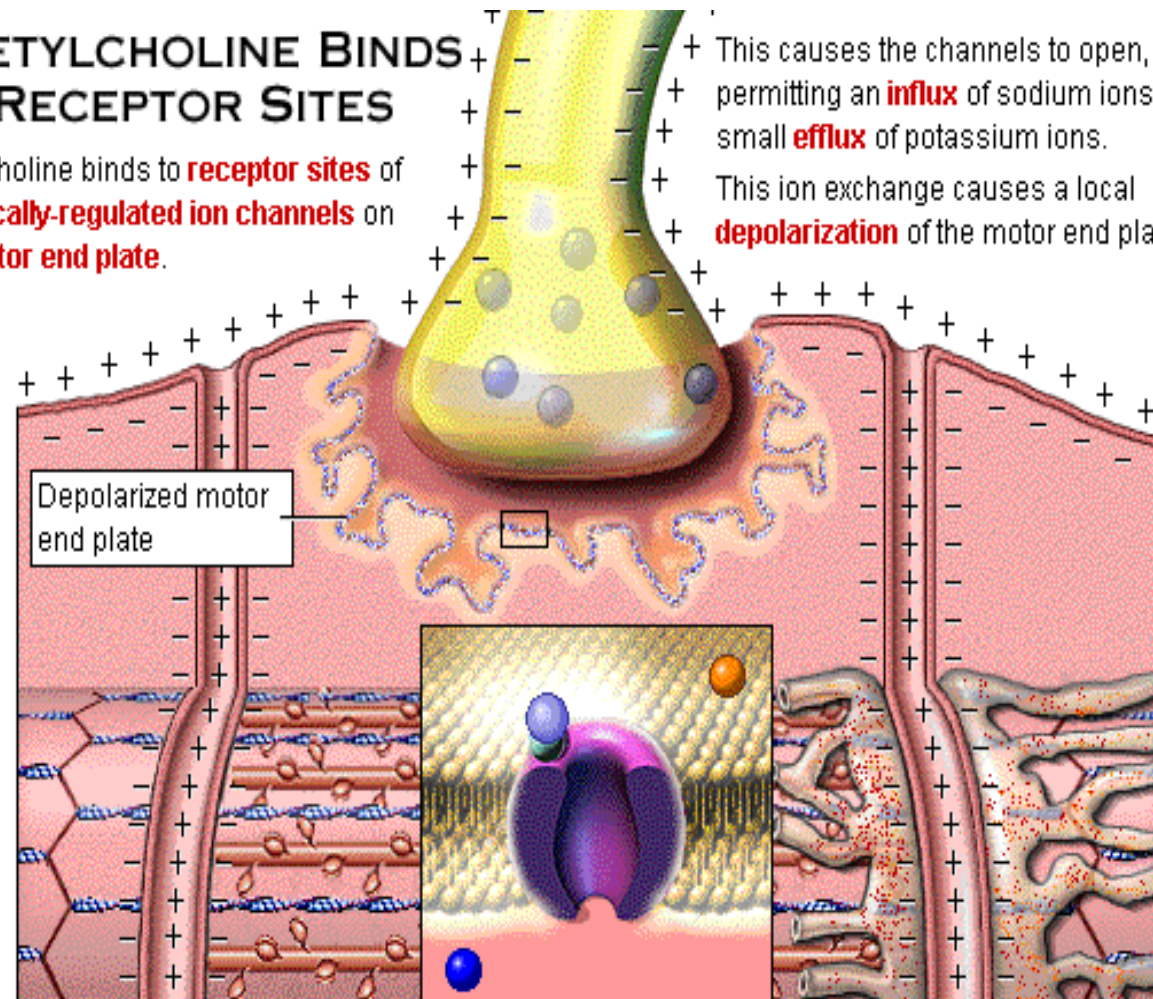
This causes the channels to open, permitting an **influx** of sodium ions and a small **efflux** of potassium ions. This ion exchange causes a local **depolarization** of the motor end plate.



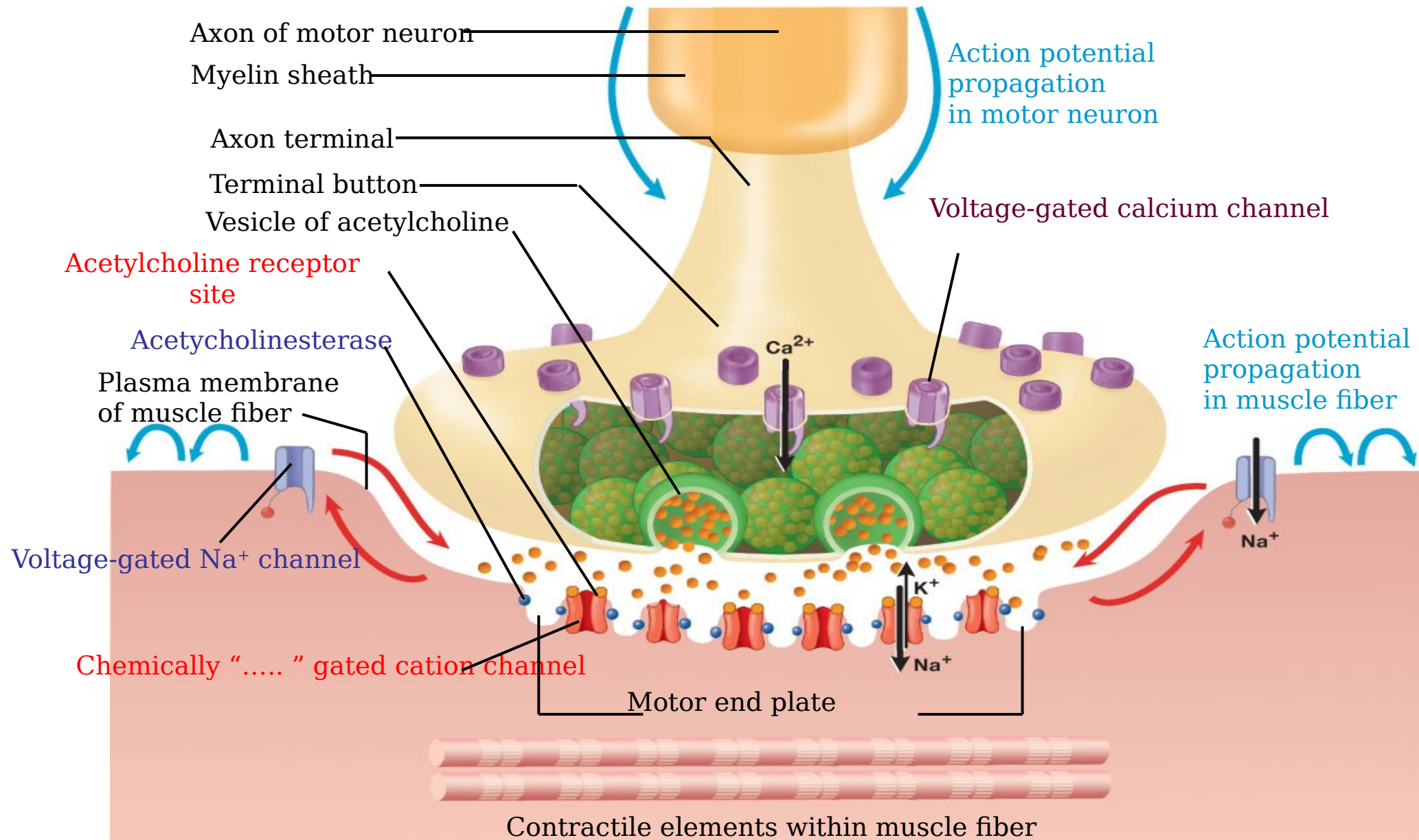
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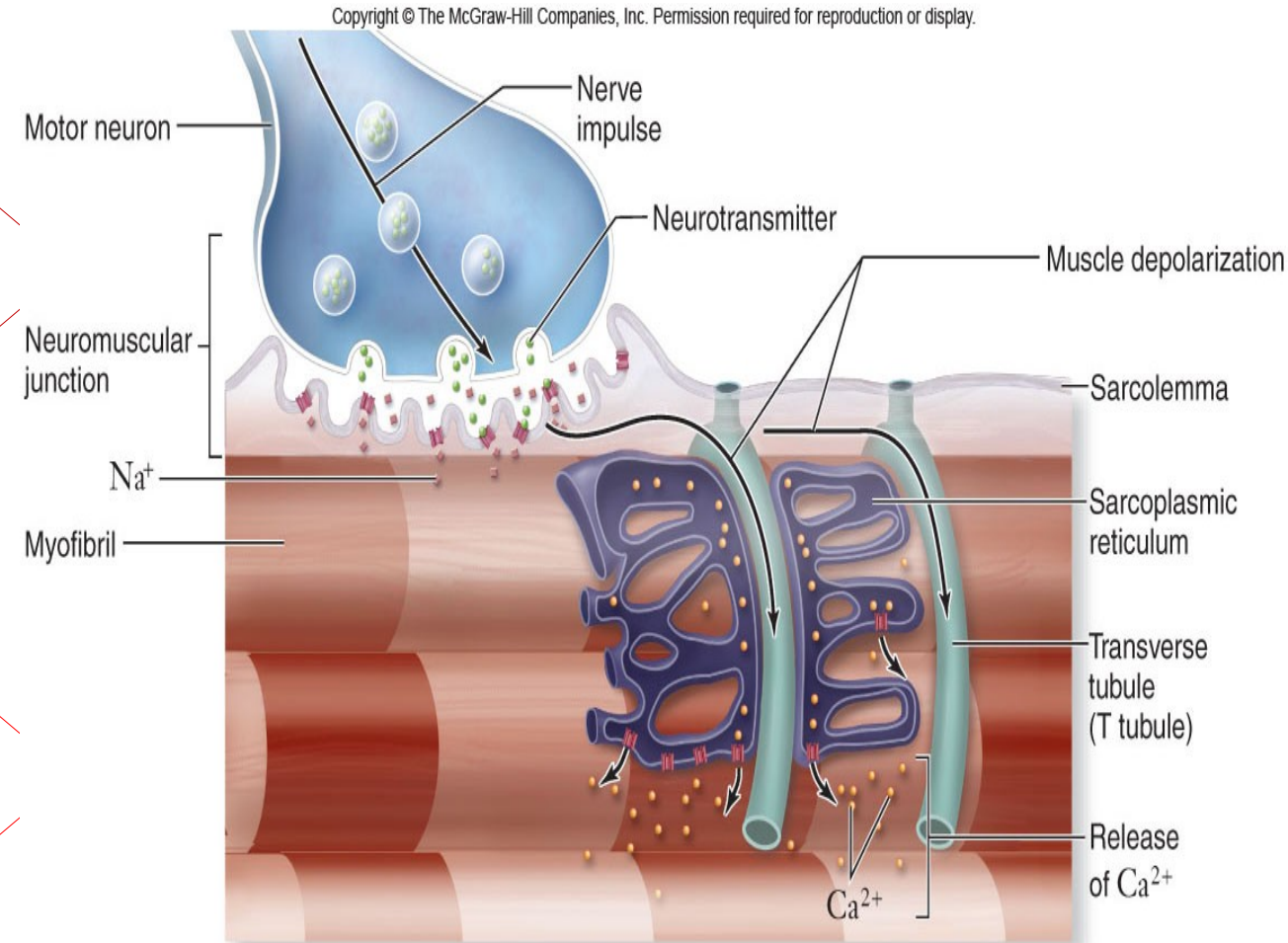






The action potential in the muscle spreads along the muscle membrane on both sides of the motor end plate

When the action potential reaches the T tubule it dips down the muscle fiber and causes release of  $\text{Ca}^{++}$  from the lateral sacs



[http://www.sps186.org/downloads/attachments/24708/chapt47\\_lecture.pdf](http://www.sps186.org/downloads/attachments/24708/chapt47_lecture.pdf)



Muscle's electrical response is turned off by an enzyme present at the motor end plate membrane which inactivates acetylcholine (ACh).

This enzyme is the acetylcholinesterase (AChE)

This terminates the action potential  
and response of the muscle cell



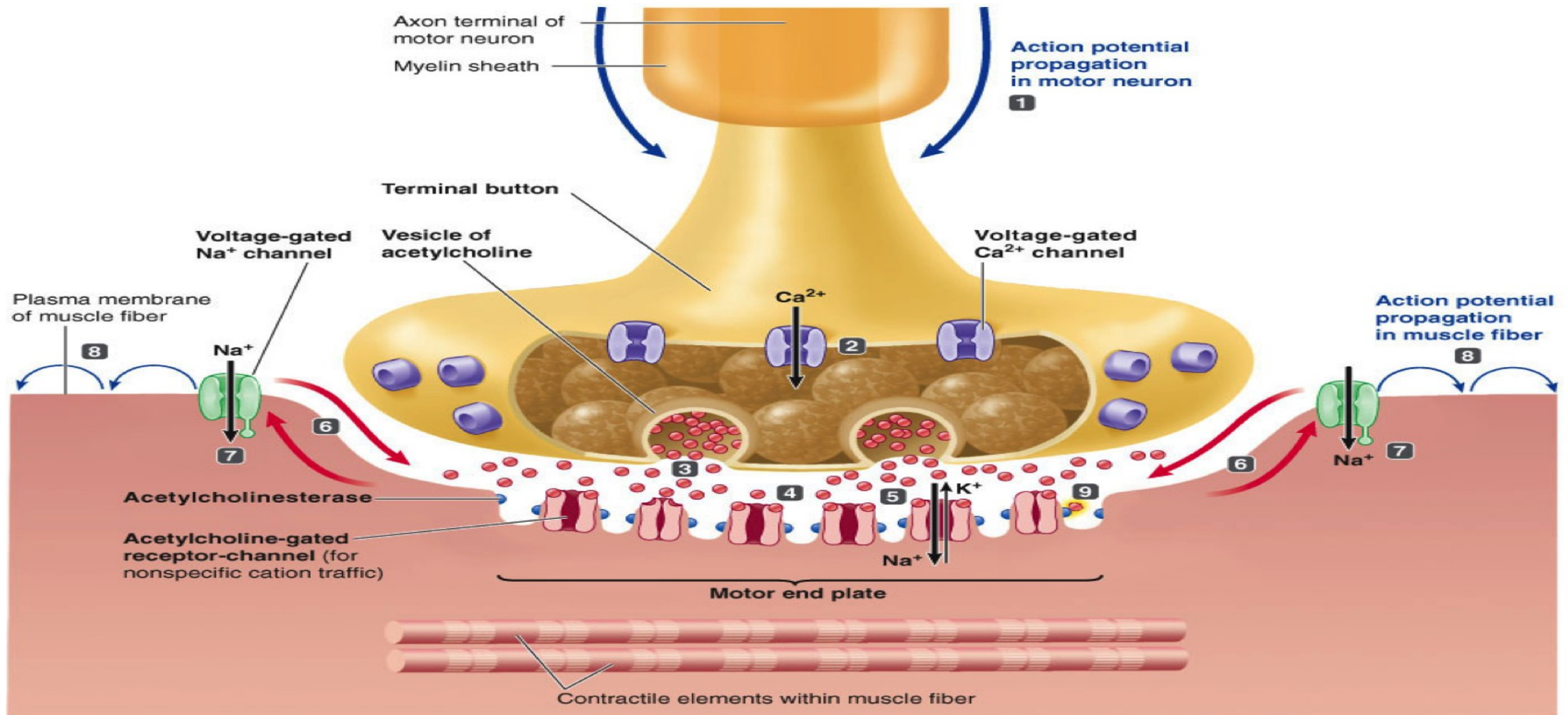
# Fate of acetyl choline (Ach)



- ❖ Acetylcholine is rapidly destroyed (after one millisecond) from its release, by the acetyl cholinesterase enzyme in the cleft itself
- ❖ This short time is sufficient for acetylcholine to exit the muscle fibers
- ❖ The rapid hydrolysis of acetylcholine prevents re-excitation of the muscle fiber after recovery from the previous action potential



# Summary for the mechanism of neuromuscular transmission



## Summary for the mechanism of neuromuscular transmission

<http://resumegold.foreignluxury.co/neuromuscular-junction/neuromuscular-junction-3>



# Properties of neuromuscular transmission



## 1. Unidirectional

- Neuromuscular transmission occurs in one direction from the nerve to the muscle and not in the opposite direction

## 2. Delay

- There is some delay about 0.5 msec. in neuromuscular transmission
- This time is used for release of acetylcholine, its passage across the synaptic cleft, its binding to the receptors at the outer surface of the membrane, depolarization occurs and E.P.P. is created till it reaches the firing level and an action potential is

generated at the muscle fiber membrane

## 3. Fatigue

- The neuromuscular junction is the first site in the neuromuscular system which suffer from fatigue




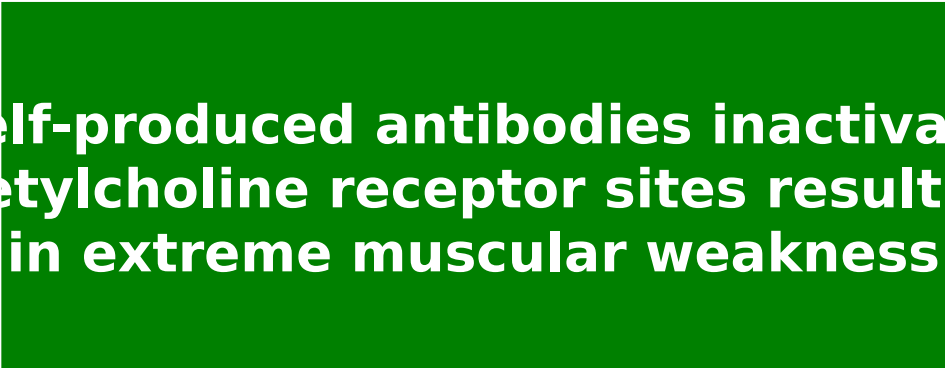
## 4. Can be stimulated or inhibited

Transmission of impulses at the MEP can be affected by certain drugs or diseases






# Chemical agents and diseases that affect neuromuscular junction



Chemical agent or disease	Mechanism (block receptors at MEP)
 <b>Curare</b>	 Reversibly binds with acetylcholine receptors. Consequently paralysis ensues
 <b>Myasthenia gravis</b>	 Self-produced antibodies inactivate acetylcholine receptor sites resulting in extreme muscular weakness



# Chemical agents and diseases that affect neuromuscular junction

Chemical agent or disease	Mechanism
 <b>Neostigmine</b>	<b>Temporarily inhibit acetylcholinesterase</b> <b>the treatment of choice in myasthenia gravis</b>
 <b>organophosphates</b>	<b>Irreversibly inhibit acetylcholinesterase</b> <b>used in pesticides and military gases (toxic)</b>
 <b>Clostridium botulinum toxin</b>	<b>Block release of acetylcholine</b> <b>No muscle activation</b>



# Complete

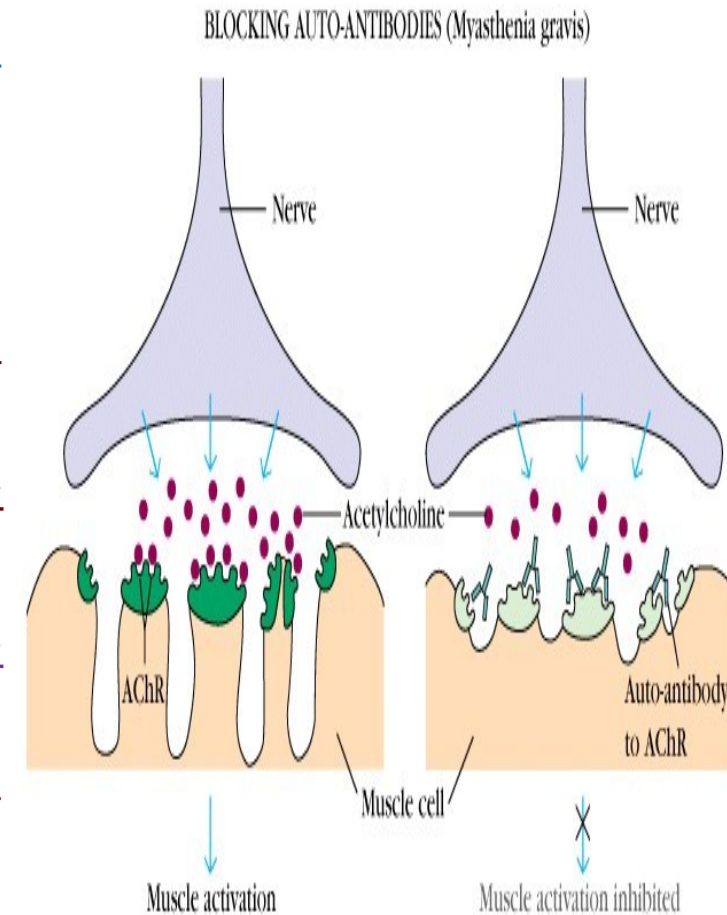
- The drug of choice in treatment of myasthenia gravis is.....
- It acts through.....



# Myasthenia gravis & its treatment



- An autoimmune disease in which some of the acetylcholine receptors are destroyed by circulating antibodies
- Acetylcholine released by the impulses can't produce an immediate effect and is destroyed by Acetyl cholinesterase
- Drugs which inhibit the action of acetylcholine esterase and allow accumulation of adequate amounts of acetylcholine to stimulate the remaining receptors can be used e.g. neostigmine



[http://www.meduniwien.ac.at/typo3/fileadmin/IPPP/Lernunterlagen\\_Prof.\\_Jensen-Jarolim/Jensen-Jarolim\\_2009\\_Autoimmune-malignant.pdf](http://www.meduniwien.ac.at/typo3/fileadmin/IPPP/Lernunterlagen_Prof._Jensen-Jarolim/Jensen-Jarolim_2009_Autoimmune-malignant.pdf)





## 1. Which of the followings best describes the end-plate potential?

- ☒ a. It is directly followed by contraction of skeletal muscle fibers.
- b. It is rapidly propagated along the muscle surface.
- c. It presents a localized state of depolarization at motor end plate.

## 2. How can acetylcholine excite a muscle fiber?

- ☒ a. It enters the muscle fiber by endocytosis.
- b. It enters the muscle fiber through protein channels.
- ☐ c. It binds to receptors in the sarcolemma of the muscle fiber.
- d. It binds to a specific carrier in synaptic cleft.







## SUGGESTED TEXTBOOKS



**USLME step 1 lecture notes physiology 2017**

<https://drive.google.com/drive/folders/1b6hSiwAzGyRypOTDCnnBw68MmQEVRv-u?usp=sharing>

**Guyton and Hall Textbook of Medical Physiology**

<https://www.amazon.com/Guyton-Hall-Textbook-Medical-Physiology/dp/1455770051>

**Ganong's Review of Medical Physiology, 25e.**

<https://www.amazon.com/Ganongs-Review-Medical-Physiology-Twenty-Fifth/dp/007182510X>

**Lippincott's Illustrated Review: Physiology**

<https://www.amazon.com/Lippincott-Illustrated-Reviews-Physiology/dp/1609132416>

**Sembulingam Essentials of Medical Physiology, 6<sup>th</sup> Edition**

[https://www.amazon.in/Books-Sembulingam/s?ie=UTF8&page=1&rh=n%3A976389031%2Cp\\_27%3A](https://www.amazon.in/Books-Sembulingam/s?ie=UTF8&page=1&rh=n%3A976389031%2Cp_27%3A)

*Thank You  
So Much*